REMARKS

Claims 1, 7, 9, 10, 13, 15, 17, 19, 21, and 23-33 are pending in the application. Claims 7, 9, 13, 15, 17, 19, 21, 23, 24, and 33 are withdrawn as being drawn to non-elected inventions. Claims 1, 10, and 25-32 are under active consideration.

Claim 1 has been amended to recite a purified polypeptide comprising the amino acid sequence of SEQ ID NO:1331, or a purified polypeptide comprising a contiguous amino acid sequence with at least 70% sequence identity to the sequence of SEQ ID NO:1331, wherein the polypeptide comprises at least one antigenic determinant that elicits an immune response against Neisserial bacteria and has a length of 100 amino acids or less Support for the amendment can be found in the specification, for example, at page 2, lines 8-10 and lines 18-21, page 3, lines 20-27; page 10, lines 28-29 and page 13, lines 24-26. Accordingly, the specification provides adequate support for the amendment. Entry of this amendment is respectfully requested.

Cancellation and amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the canceled or unamended claims.

Restriction Requirement

Applicants affirm the election with traverse of Group I, which corresponds to claims 1, 10, and 25-33 drawn to antigenic polypeptides. Applicants submit that claims 9 and 17 drawn to nucleic acids encoding the antigenic polypeptides of Group I, according to the unity of invention standard, should be examined with the elected claims currently under examination.

The unity of invention standard *must* be applied in national stage applications

Section 1850 of the Manual of Patent Examining Procedure (original 8th edition, published August, 2001) (hereinafter "MPEP") provides:

> ... [W]hen the Office considers international applications ... during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111....

> In applying PCT Rule 13.2 to ... national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2....

Id at page 1800-60 to -61.

MPEP section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

> Examiners are reminded that unity of invention (not restriction) practice is applicable ... in national stage (filed under 35 U.S.C. 371) applications.

Id at page 1800-149, column 1.

Unity of Invention is accepted between claims to polypeptides and claims to the nucleic acids which encode them

Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT provides that unity of invention is accepted between a protein and the nucleic acid that encodes it:

> *Example 17*
> Claim 1: Protein X.
> Claim 2: DNA sequence encoding protein X.
> Expression of the DNA sequence in a host results in the production of a protein which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity between claims 1 and 2 is accepted.

Applicants, therefore, request that the Examiner withdraw the Restriction Requirement at least with respect to claims 9 and 17 of Group II, and examine those claims together with the elected polypeptide claims of Group I. As currently amended, the claims of Group I drawn to polypeptides and the claims of Group II drawn to nucleic acids do not encompass prior art; therefore, the "objection of lack of unity" based on the reference of Relf et al. (J. Clin. Microbiol. 30:3190-3194, 1992) is not applicable. Applicants submit that unity of invention exists for

claims drawn to the polypeptide sequence of SEQ ID NO:1331 (*i.e.*, claims 1, 10, and 25-33) and claims drawn a nucleic acid encoding it (*i.e.*, claims 9 and 17) based on the rules concerning unity of invention under the Patent Cooperation Treaty.

Rejoinder

Applicants request that claims 13, 24, and 33, drawn to methods of using the antigenic polypeptides, be rejoined per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products. Applicants request that claims 13, 24, and 33 be rejoined and examined upon allowance of any of the claims drawn to the antigenic polypeptides of Group I.

Objections to the Specification

Trademarks

The specification has been amended to properly recite trademarks with marks capitalized and accompanied by generic terminology. Withdrawal of the objection to the Specification is therefore respectfully requested.

ATCC Address

The specification has been amended to correct the address of the American Type Culture Collection. Withdrawal of the objection to the Specification is therefore respectfully requested.

Rejection under 35 U.S.C. § 101

Claim 1 and its dependent claims have been rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter on the grounds that "[c]laim 1 is drawn to a polypeptide, and therefore reads on products of nature, i.e., naturally occurring polypeptide" (Office Action, page 4). However, claim 1 recites that the polypeptide "has a length of 100 amino acids or less." It is believed that such polypeptides recited by claim 1 do not exist in

nature. Regardless, claim 1 has been revised to recite a "purified polypeptide." Support for this amendment can be found in the specification, for example, at page 2, lines 18-21, page 10, lines 28-29, and page 13, lines 24-26. For at least these reasons, withdrawal of the rejection under 35 U.S.C. § 101 is respectfully requested.

New Matter Rejection under 35 U.S.C. § 112, first paragraph

Claim 1 and its dependent claims have been rejected under 35 U.S.C. § 112, first paragraph as allegedly "containing subject matter which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (Office Action, page 4). In particular, the Office Action alleges that there is no descriptive support for the new limitation, "a polypeptide comprising a contiguous amino acid sequence with at least 50% sequence identity to SEQ ID NO:1331" that was introduced by amendment. Applicants respectfully disagree and traverse the rejection.

Claim 1, as currently amended, recites "a purified polypeptide comprising a contiguous amino acid sequence with at least 70% sequence identity to SEQ ID NO:1331." The specification provides adequate support for the claimed variants. See the specification, for example, at page 2, lines 7-10, which describes variant polypeptides that are homologous to fragments of the protein (ORF114-1) disclosed in international patent application WO99/36544:

> The invention also provides polypeptides that are homologous (i. e. have sequence identity) to these fragments. Depending on the particular fragment, the degree of sequence identity is preferably greater than 50% (e. g. 60%, 70%, 80%, 90%, 95%, 99% or more). These homologous polypeptides include mutants and allelic variants of the fragments.

Fragments of ORF114-1 are disclosed in Table I at pages 64-71 and include fragment 1331 (Table I at page 67) corresponding to a polypeptide comprising the sequence of SEQ ID NO:1331.

Applicants submit that no new matter was added by the previous amendment or by the present amendment and withdrawal of the new matter rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

Written Description Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 10, and 25-32 have been rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of an adequate written description. In particular, the Office Action alleges that "the instant specification fails to teach a single variant of a polypeptide sequence having 50 to 99% identity to the amino acid sequence of SEQ ID NO:1331 and concurrently having the antigenic, diagnostic, prophylactic and therapeutic activity" (Office Action, page 5). The Office Action further alleges that "Applicants have not shown that variation or modification of a reference sequence encoding a polypeptide would automatically predict the production of a polypeptide variant as claimed having the specific antigenic and therapeutic functional activities." (Office Action, page 6). The Office Action further alleges that "[w]ith the exception of the polypeptide of SEQ ID NO:1331, a skilled artisan cannot envision the detailed chemical structure of all the polypeptide variant species encompassed by the recited molecule" (Office Action, page 6). Applicants respectfully traverse the rejection on the following grounds.

The fundamental factual inquiry in written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976). It is not necessary that the application describe the claimed invention *in ipsis verba.* Rather, all that is required is that the specification reasonably convey possession of the invention. *See, e.g., In re Lukach,* 169 USPQ 795, 796 (CCPA 1971). Finally, determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange,* 209 USPQ 288 (CCPA 1981).

Furthermore, the Patent Office's own guidelines on written description are clear -- the written description requirement is highly fact-dependent and there is a strong presumption that an adequate written description of the claimed invention is present at the time of filing:

> [t]he description need only describe in detail that which is new or not conventional. This is equally true whether the claimed invention is a product or a process. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics. ... A "representative number of species" means that the species that are adequately described are representative of the entire genus. ... What constitutes a "representative number" is an inverse function of the skill and knowledge of the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. ... Description of a representative number of species does not require the description be of such specificity that it would provide individual support for each species that the genus embraces. (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added).

Simply put, there is absolutely **no** requirement that Applicants exemplify (or reduce to practice) every sequence falling within the scope of the claims in order to adequately describe the meningococcal variant polypeptides as claimed. Rather, the test is whether the specification contains sufficient disclosure regarding structural and functional characteristics of the claimed sequences to satisfy the written description requirement. In the pending case, the specification as filed more than adequately describes the structure and function of the claimed polypeptides.

The Scope of the Claims

Because any written description inquiry must begin with claim construction, it is important to note at the outset of this discussion that the claims are not as broad as painted by the Examiner. Moreover, the claims clearly recite both the structure (sequence SEQ ID NO:1331) and function (elicits an immune response against Neisserial bacteria) of the recited polypeptides. Therefore, when properly construed, it is plain that only polypeptide sequences having the recited structure and function are encompassed by the pending claims.

With regard to the Examiner's contention that a convincing structure-function relationship has to exist between the structure of a polypeptide variant and the function of the polypeptide variant, Applicants note that a correlation between polypeptide structure (primary

sequence or tertiary structure) and antigenic function indicates that antigenic polypeptides can tolerate many modifications. In other words, whereas essential residues are readily identifiable for enzymatic (*e.g.,* catalytic) functions, a polypeptide can tolerate multiple substitutions at various residues while still retaining its antigenic function.[1] The written description requirement is satisfied because the specification describes sufficient structural and functional characteristics of the claimed molecules.

The Specification Describes the Claimed Subject Matter

The specification as filed fully describes the claimed subject matter. The specification describes, in detail, how antigenic meningococcal polypeptides that elicit immune responses to Neisserial bacteria are identified (See specification, *e.g.,* page 37, lines 9-29). Further, the sequences of various antigenic meningococcal polypeptides are described (See, *e.g.,* Table I). With regard to percent identity, the specification clearly describes how to determine percent identity between polypeptides, for example, in the text beginning on line 9 of page 2. Performing such alignments is routine and conventional. Any polypeptide exhibiting the requisite 70% identity can be readily evaluated for antigenicity as described, for instance, in the specification as filed (See, *e.g.,* page 37, lines 9-29).

It is axiomatic that the specification need only describe in detail that which is new or not conventional. (See, Guidelines on Written Description, page 275). In the case at hand, a skilled artisan reading the specification would have known that Applicants were in possession of claimed polypeptides as recited in the claims in view of the specification's extensive disclosure of (1) precise sequences falling in the scope of the claims; (2) conventional, known methods of aligning polypeptides; and (3) conventional, known methods of testing the polypeptides for antigenicity. In view of the disclosure of the specification and state of the art, it would have been plain to the skilled artisan that Applicants were in possession of the claimed invention at the time the specification was filed.

[1] Nor does antigenic function necessarily depend on tertiary structure. Simply put, wild type folding is not critical to generating an immune response and, accordingly, the references cited on pages 8 and 9 of the Office Action are not relevant to the enablement or written description inquiry.

Representative Species

Turning now to the Office's assertion that there are insufficient representative species described in the specification to adequately describe the alleged "broad genus" of polypeptides, Applicants note that a "representative number" does not mean that each and every species falling within the genus must be disclosed. For the reasons noted above, it is well within the purview of the skilled artisan, in view of the teachings of the specification, to align polypeptide sequences and determine those having the requisite similarity to SEQ ID NO:1331. (See specification, *e.g.*, at page 2, lines 10-13). Accordingly, the representative number of species disclosed in the specification more than adequately conveys to the skilled artisan that Applicants were in possession of the precisely claimed molecules at the time the application was filed.

Moreover, the USPTO's own training materials on the application of the Written Description Guidelines permit claims to a genus of polypeptide variants without requiring that the actual amino acid sequence of every variant be disclosed. A reference sequence is considered to be "representative of the genus" when all members have a specified percentage identity and specified activity that defines the "common attributes possessed by members of the genus" (see Revised Interim Written Description Guidelines Training Materials, "Synopsis of Application of Written Description Guidelines," Example 14: Product by Function). Thus, the claimed genus of antigenic meningococcal variant polypeptides that elicit immune responses to Neisserial bacteria are adequately described.

The Cases Cited are Not Applicable

Furthermore, the Office's reliance on *Fiers v. Revel* and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* is misplaced. The written description requirement of section 112 is highly fact dependent and the claims, disclosure and state of the art in *Fiers* and *Amgen* are entirely different from those in the case at hand. Indeed, the specification and claims at issue in either *Fiers* or *Amgen* were defective because they were devoid of any structure (sequence) disclosure. In contrast, Applicants' specification as filed and pending claims contain and recite ample structural and functional characteristics.

Furthermore, the Federal Circuit's holdings in *Fiers* or *Amgen* in no way necessitate that the claims be limited in scope to those sequences disclosed in SEQ ID NOs. Indeed, in *Fiers v.*

Revel, the Federal Circuit indicated that, although disclosure of a method of isolating DNA did not adequately describe the DNA, the DNA itself may be properly defined by one or more of the following parameters: "structure, formula, chemical name or physical properties." Thus, it is possible that DNA can be entirely described by its physical properties, *i.e.* by function. Again, Applicants' disclosure and claims include both structure and physical properties and, accordingly, the cases cited by the Office are not relevant to the case at hand.

The present application has a priority date of July 14, 1999. Much has happened in the development of recombinant DNA technology in the 15 or more years from the time of filing of the applications involved in *Fiers* and *Amgen* and the present application. For example, the technique of polymerase chain reaction (PCR) was developed. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:1331 and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polypeptide variants at the time of filing of this application.

For at least the above reasons, withdrawal of the written description rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Enablement Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 10, and 25-32 have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not provide an enabling disclosure commensurate in scope with the claims. In particular, the Examiner alleges that "the specification, while being enabling for an isolated fragment of a meningococcal protein wherein the fragment has the amino acid sequence of SEQ ID NO:1331, does not reasonably provide enablement for a polypeptide comprising a contiguous amino acid sequence with 'at least 50% sequence identity to SEQ ID NO:1331', wherein the polypeptide comprises at least one antigenic determinant and has a length of 100 amino acids or less, as claimed" (Office Action, page 6). The Office Action further cites Burgess et al. (1990) J. Cell Biol. 111:2129-2138; and Lazar et al. (1988) Mol. Cellular Biol. 8:1247-1252 in support of the position that "it is unlikely that a polypeptide molecule having as

much as 50% dissimilarity with the 18 amino acid-long native polypeptide of SEQ ID NO:1331 as recited, would have its primary, secondary or tertiary structure unchanged such that it contains at least one antigenic determinant containing a B-cell epitope and a T-cell epitope and would have the required biologic activities retained" (Office Action, page 8). Applicants respectfully traverse the rejection on the following grounds.

As set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be take as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Undue experimentation is not required to practice the claimed invention because the claims are enabled throughout their scope and, in addition, the references cited by the Examiner do not in any way establish unpredictability. When the *Wands* factors are considered, it is clear that the specification as filed fully enables the pending claims throughout their scope.

Applicants note that claim 1, as amended, recites "a purified polypeptide comprising a contiguous amino acid sequence with at least 70% sequence identity to the sequence of SEQ ID NO:1331, wherein the polypeptide comprises at least one antigenic determinant that elicits an immune response against Neisserial bacteria and has a length of 100 amino acids or less." Thus the limitations of the claims do not require that the antigenic polypeptides have "all the functional or biological properties of the native protein from which the fragment, SEQ ID NO:1331 was obtained. A correlation between polypeptide structure (primary sequence or tertiary structure) and immunogenic function indicates that antigenic polypeptides can tolerate many modifications.

The Examiner has asserted that "undisclosed and unidentified functional polypeptide molecules of at least 50% sequence identity encompassed in the claims are not enabled for their

scope" (Office Action, page 10). This is not a correct application of the law. Applicants are under no legal obligation to teach each and every member of a claimed genus. Rather, for a claimed genus, representative examples together with a statement applicable to the genus as a whole are sufficient to establish enablement if the skilled artisan would expect the claimed genus could be used in the manner set forth. *See, e.g.,* U.S. Patent and Trademark Office's Training Materials on Enablement, p. 29.

Given the information provided by SEQ ID NO:1331, one of skill in the art would be able to routinely identify "a polypeptide comprising a contiguous amino acid sequence with at least 70% sequence identity to the sequence of SEQ ID NO:1331." See specification, for example, on page 2, lines 10-13, where it is noted how to determine sequences falling within the requisite percent identity. At the time of filing of the instant application, determining sequence identity was utterly routine. Furthermore, the specification also provides guidance on how to make the claimed polypeptide variants. For example, the specification describes how to make the polypeptides by recombinant expression or chemical synthesis. See, *e.g.*, page 2, lines 18-22, page 5, line 21 through page 21, line 3. The identification of relevant polynucleotides encoding the variant polypeptides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed. See, *e.g.*, page 34, line 10 through page 35, line 25 and page 36, lines 26-33. The specification further provides guidance on methods of identifying antigenic polypeptides (*e.g.*, page 37, lines 9-29) and methods of using antigenic polypeptides to produce antibodies (*e.g.*, page 21, line 5 through page 22, line 18), in immunogenic compositions such as vaccines (*e.g.*, page 23, line 25 through page 25; line 15), and in immunodiagnostic assays (*e.g.*, page 33, line 27 through page 34, line 8). Thus, the specification provides ample guidance as to methods of identification, generation, and use of the antigenic polypeptides of the claimed invention.

The Cited References Do Not Establish Unpredictability

The Examiner has cited certain references (Burgess et al., 1990; Lazar et al., 1988; and Bowie et al., 1990) as allegedly establishing the unpredictability of the art relevant to the claimed invention. Specifically, the Office Action asserts that these references demonstrate that it would require undue experimentation to determine which molecules exhibiting 70% identity to SEQ ID

NO:1331 encode an antigenic polypeptide that elicits an immune response to Neisserial bacteria. (Office Action, pages 8-9). However, upon careful review, it is clear that these references are not relevant to the claimed subject matter.

First, the Office action alleges that protein chemistry is unpredictable and "[a]n alteration in a single amino acid can eliminate or drastically change one or more functions(s) of the polypeptide" (Office Action, page 8). However, the cited references of Burgess et al. and Lazar et al. are irrelevant to the claimed invention. Both references describe the effects of mutations on the biological activities of growth factors, *i.e.* acidic fibroblast growth factor and TGF-α, respectively. The references do not describe the effects of mutations on antigenic function. Again, the claimed antigenic variant polypeptides are not required to retain all the functional or biological properties of the native protein, but rather, are only required to have antigenic function, that is, the ability to elicit an immune response against Neisserial bacteria. Polypeptides can tolerate multiple substitutions at various residues while still retaining antigenic function. One of skill in the art can routinely produce antigenic polypeptides, and polypeptides that are not antigenic and that do not elicit an immune response to Neisserial bacteria are not encompassed by the claims.

To further support an assertion that undue experimentation would be required to derive the claimed polypeptides, the Office Action cites Bowie et al. (Science 247:1306-1310, 1990). The Examiner's position regarding Bowie appears to be that because there may be sequences that exhibit the requisite homology, but are not antigenic polypeptides that elicit an immune response to Neisserial bacteria (for example, because the structure of the polypeptide they encode is not predictable), undue experimentation would be required to make and use the claimed antigenic polypeptides. (Office Action, page 9). This reasoning is entirely improper. Sequences that do not produce antigenic polypeptides that elicit an immune response to Neisserial bacteria are not encompassed by the claims. Applicants also respectfully point out that it is not necessary to predict a protein's structure in order to elicit an immune response to a protein. Contrary to the Office Action's assertions, production of antibodies to an antigen is routinely practiced in the absence of knowledge of a protein's structure. One of skill in the art can routinely produce antibodies that specifically bind to a protein by immunizing an appropiate host with oligopeptide fragments of that protein. It is well known in the art that it is possible to produce antibodies to

almost any part of an antigen, and is not especially difficult to obtain antibodies with specificity for a particular protein. The specification provides sufficient guidance for one of skill in the art to elicit an immune response with the recited antigenic polypeptides. See specification, e.g., at pages 21-22, and page 33, line 27 through page 34, line 4).

Further, it is well settled that time-consuming or expensive experimentation is **not** undue if it is routine. (See, *e.g.,* PTO Training Manual on Enablement, pages 30-31, citing *United States v. Telectonics Inc.,* USPQ2d 1217, 1223 (Fed. Cir. 1988), *cert. denied* 490 U.S. 1046 (1989) holding the disclosure of a single exemplified embodiment and a method to determine other embodiments was enabling, even in the face of evidence that determining additional embodiments might require 6-12 months of effort and cost over $50,000). Thus, the possibility of generating inoperative embodiments, allegedly established by the cited references discussed above, is not relevant to the claimed invention.

Furthermore, the presence of inoperative embodiments does not necessarily render a claim nonenabled. *See, e.g.,* MPEP § 2164.08(b); and *In re Angstadt,* 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976. The test of enablement is not what is predictable *a priori*, but what the specification teaches the skilled practitioner in regard to the claimed subject matter. Thus, not every species (or even a majority of species) encompassed by the claims, even in an unpredictable area like the chemical sciences, needs to be disclosed. *In re Angstadt,* 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976. The notion that one of ordinary skill in the art must have reasonable assurances of obtaining positive results on every occasion has been emphatically rejected. *Angstadt* at 219. So long as it is clear that some species render the claims operative, the inclusion of possible inoperative species cannot invalidate the claim under paragraph 1 of 35 U.S.C. §112. *See, also, In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, CCPA 1971; *Horton v. Stevens*, 7 USPQ2d 1245, 1247, Fed. Cir. 1988.

In the pending case, Applicants again note that every single polypeptide species exhibiting 70% identity to SEQ ID NO:1331 can be determined *a priori* and, as such, the entire genus of polypeptides exhibiting 70% identity to SEQ ID NO:1331 is enabled by the specification as filed.[2] Thus, there are no inoperative "structural" embodiments encompassed by

[2] Applicants also direct the Examiner's attention to Example N:DNA of the Patent Office's "Training Materials for Examining Patent Applications with respect to 35 U.S.C. § 112, First Paragraph -- Enablement --

the claims and, as such, the specification clearly enables the structures (sequences) of the claims.

Moreover, as set forth in the case law described above, the possibility that there may be some inoperative "functional" embodiments (*e.g.,* some of the polypeptides may not elicit an immune response to Neisserial bacteria) does not render the specification nonenabling because the specification clearly teaches how to identify antigenic polypeptides and testing for immunogenicity is utterly routine. Therefore, routine experimentation, as would be required to determine if an embodiment falls within the "functional" scope of the claims, is not undue experimentation.[3]

Thus, not only does the claim language itself exclude inoperative embodiments, namely any and all polypeptides that do not elicit an immune response to Neisserial bacteria, the experimentation needed to identify inoperative embodiments is not undue. Accordingly, the presence of potentially inoperative functional embodiments cannot form grounds for rejecting the pending claims as allegedly nonenabled.

The question of enablement is what the specification teaches one of skill in the art. In this case, the specification teaches one of skill in the art how to make and use the precisely claimed invention. Indeed, Applicants have repeatedly pointed to specific disclosures (including working examples) that establish enablement.

Applicants further note that there is no requirement under the law to provide "working examples." As set forth in *In re Borkowski,* 164 USPQ 642, 645 (CCPA 1970) (footnote omitted):

> However, as we have stated in a number of opinions, a specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation.

See also M.P.E.P. 2164.02 as follows:

Chemical/Biotechnical Applications," which states that even with a very large genus of sequences (at least 1.26 x 10^{21}), undue experimentation is not required to determine all members of the genus because "each embodiment can be readily identified using the genetic code, synthesized using conventional methods, and used in the manner taught in the specification." see, page N-4.

[3] *See, also, United States v. Telectronics Inc.,* 8 USPQ2d 1217 (Fed. Cir. 1988), *cert. denied,* 490 U.S. 1046 (1989)), holding that routine experimentation, even if extensive (on the order of six or more months and tens of thousands of dollars), is not necessarily undue.

> Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. An example may be "working" or "prophetic"... A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved.

Thus, there is no requirement under the law to provide "working examples" of what is claimed. Rather, one looks to whether the specification provides a description of how to make and use what is claimed. The present specification provides the requisite description.

Contrary to the standard set forth in *Marzocchi* and *Borkowski*, the Examiner has failed to provide any ***reasons*** why one would doubt that the guidance provided by the present specification would enable one to make and use the recited meningococcal polypeptides. Hence, a *prima facie* case for non-enablement has not been established. For at least the above reasons, withdrawal of the enablement rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1, 10, and 25-32 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." (Office Action, pages 10-11).

(a) The Examiner alleges that "[c]laim 1 lacks proper antecedent basis in the limitation: 'SEQ ID NO:1331' (see lines 3 and 4)" (Office Action, page 10). To expedite prosecution, claim 1 has been amended to recite "a polypeptide comprising a contiguous amino acid sequence with at least 70% sequence identity to the sequence of SEQ ID NO:1331" to further clarify antecedent basis.

(b) The Examiner further alleges that "[c]laims 10 and 25-32, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim" (Office Action, page 10). In view of the amendment of claim 1, Applicants respectfully request withdrawal of the rejection on this basis for at least the reasons stated above.

For at least these reasons, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

Rejections under 35 U.S.C. § 102 and § 103

Claims 1 and 25-28 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by the reference of Relf et al. (J. Clin. Microbiol. 30:3190-3194, 1992). In particular, the Office Action alleges that "Relf et al. disclosed a 59 amino acid-long polypeptide having a contiguous amino acid sequence, KAAWLNQKSKELE, with at least 50% sequence identity to the instantly recited SEQ ID NO:1331" and that "[t]he prior art polypeptide comprises a 5-amino aid-long [sic] KAAWN, and a 4-amino acid-long KELE antigenic determinant" (Office Action, page 11). In addition, claims 10 and 29-32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the reference of Relf et al. (J. Clin. Microbiol. 30:3190-3194, 1992) on the grounds that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add an art known or art available pharmaceutically acceptable vehicle such as saline or water, to Relf's polypeptide to produce the instant invention, with a reasonable expectation of success" (Office Action, page 12).

For a reference to anticipate claimed subject matter under 35 U.S.C. § 102, "the reference must teach every aspect of the claimed invention either explicitly or implicitly." M.P.E.P. § 706.02. Applicants respectfully submit that the reference of Relf et al. does not teach or suggest all aspects of the Applicants' invention, either explicitly or implicitly.

Claim 1, as currently amended, recites "a purified polypeptide comprising a contiguous amino acid sequence with at least ***70%*** sequence identity to the sequence of SEQ ID NO:1331, wherein the polypeptide comprises at least one antigenic determinant that elicits an immune response against Neisserial bacteria and has a length of 100 amino acids or less." The reference of Relf et al. does not disclose a polypeptide comprising a sequence with at least 70% identity to the sequence of SEQ ID NO:1331, nor compositions containing such polypeptides and a pharmaceutically acceptable vehicle. Therefore, the reference of Relf et al. fails to teach or suggest all the limitations of the claims, and withdrawal of the rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) is respectfully requested.

CONCLUSION

In light of the above remarks, Applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

Please direct all further written communications regarding this application to:

Alisa Harbin, Esq.
Chiron Corporation
Intellectual Property - R440
P. O. Box 8097
Emeryville, CA 94662-8097
Tel: (510) 923-2708
Fax: (510) 655-3542

Respectfully submitted,

Date: June 21, 2005

By: Jenny Buchbinder
Jenny Buchbinder, Ph.D.
Registration No. 48,588
(650) 354-3383

CHIRON CORPORATION
Intellectual Property - R440
P. O. Box 8097
Emeryville, CA 94662-8097